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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,994	07/13/2001	Johannes Gerardus Kusters	2000.566 US	3816

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PATENT DEPARTMENT
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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/904,994	KUSTERS ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

All prior claims have been canceled.
New claims 60-81 have been entered.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 9, 2007 has been entered.

Response to Arguments for Objections/Rejections Maintained

1. Applicant's arguments filed February 9, 2007 have been fully considered but they are not persuasive.

2. Applicant states the claims have been amended and submit the application is in condition for allowance.

3. In light of various amendments of the claims, some of the objections and rejections have been obviated, but others will be maintained and addressed below.

4. ***Claim Rejections - 35 USC § 112 Maintained (gene therapy, nucleic acid immunization compositions):***

The rejection of claims67-70 as previously applied to claims 46-49 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is herein maintained.

5. It is the position of the examiner that the nucleic acid molecules contained in the compositions of claims 67-70 would not induce an immune response to Helicobacter felis polypeptide, the coding sequence of SEQ ID NO 1, absent specific regulatory sequences being in association with SEQ ID NO 1, so it would not only be transcribed, but translated and secreted so an immune response could be generated. The term gene therapy is a broad term that encompasses replacement of defective genes, but also includes DNA vaccines that will transform a eukaryotic cell in a mammal which in turn will express the heterologous nucleic acid. Baird et al (2004) utilized Ig signal sequence together with epitopes to insure secretion by a mammalian cell. The instantly claimed compositions do not comprise any of the critical components to insure induction of an immune response to Helicobacter felis urease polypeptide. The claims now pending are directed to bacterial nucleic acid sequences that in and of themselves would not induce an immune response that is specific to Helicobacter felis urease based upon any of the nucleic acid sequences being directly administered to the blood stream of an animal and the claims do not recite any structural regulatory elements to insure the induction of an immune response if and when the nucleic aid molecule were taken up by the appropriate eukaryotic cell to insure the encoded polypeptide is expressed to induce an immune response. Numerous factors complicate the gene therapy art which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ dramatically based on the vector used, the protein being produced, and the disease being treated. With respect to claim 48, it was noted that HIV viral epitopes are defined within the scope of the claim to induce an immune response to HIV and to serve as a vaccine (instant Specification, page 7, paragraph 1). Bourinbaiar et al (2006) states that proposed vaccines for HIV "have shown little evidence of clinical efficacy (see abstract)." No known HIV vaccines are known "as a result of vaccination, the clinical improvement has been seldom observed."

6. While the instant Specification does provide guidance for the construction of recombinant host cells that recombinantly/heterologous express the encoded H. felis nucleic acid (see instant Specification page 4, lines 28-49 and page 5, lines 6-21), what is now claimed is an immunogenic composition that comprises the coding sequence for H.felis polypeptide, a prokaryotic coding sequence which does not naturally comprise the necessary promoters, polyA, and other regulatory sequences to successfully have the bacterial nucleic acid translated into a polypeptide and secreted into the immunocompetant host animal and to serve as a DNA vaccine/immunogenic composition. Permin et al (2005, page 21, col.1, p. 1) teaches that "genetic difference in the individual immune responses to the pathogen, for example linked to IL-1 gene cluster polymorphism, may result in failure to eradicate the infection and lead to chronic mucosal inflammation

Therefore, even if the specification is enabled the construction of the gene delivery vehicle comprising a cell targeting element, in the absence of particular guidance, the artisan would have been required to develop *in vivo* and *ex vivo* means of practicing the claimed methods and such development in the nascent and unpredictable gene/vaccine therapy art would have been considered to have necessitated undue experimentation on the part of the practitioner.

With respect to the cited references:

- Hasan et al (Exhibit A) summarized various vector mediated delivery systems for expression of a heterologous immunogen, and describes various promoters, plasmids, viral vectors, bacterial vectors for delivery of foreign encoded nucleic acids; Applicant's claims are directed to only a nucleic acid molecule and is not in association with a promoter, plasmid or vector construct as described by Hasan. The term "naked DNA" in Hasan is a plasmid that encodes a heterologous coding sequence (see page 3, section 2), as compared with the coding sequence being inserted into a viral vector (see page 7, section 3.1.1, Hasan et al) or attenuated bacterial vectors (see Hasan et al, page 7, section 3.2). Exhibit A does not present evidence commensurate in scope with the instantly claimed invention as now claimed.

- Todoroki et al (2000) utilized a plasmid to express the coding sequence for H.pylori; the compositions of instant claims 46-49 do not comprise an eukaryotic promoter, plasmid, viral vector or attenuated bacteria for the expression H. felis urease. Exhibit B does not present evidence commensurate in scope with the instantly claimed invention as now claimed.
- Miyashita et al (2002) utilized a plasmid to express the coding sequence for H.pylori; the compositions of instant claims 46-49 do not comprise an eukaryotic promoter, plasmid, viral vector or attenuated bacteria for the expression H. felis urease. Exhibit C does not present evidence commensurate in scope with the instantly claimed invention as now claimed.
- Hatzifoti et al (2004) utilized a plasmid to express the coding sequence for H.pylori; the compositions of instant claims 46-49 do not comprise an eukaryotic promoter, plasmid, viral vector or attenuated bacteria for the expression H. felis urease. Exhibit D does not present evidence commensurate in scope with the instantly claimed invention as now claimed.

The rejection under 35 USC 112, first paragraph, over claims directed to and encompassing DNA vaccines/gene therapy is maintained for reasons of record, and responses set forth herein.

7. ***Claim Rejections - 35 USC § 112*** Claims 60-81 are rejected under 35 U.S.C. 112, first paragraph as previously applied to claims 23, 26, 28, 30-34, 37-39, 40, 44, 46-50, 57-59, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed. It is the position of the examiner that while claims directed to isolated and purified nucleic acid consisting of SEQ ID NO 1, 2 and 3 has been described, the instant claimed variants that need only share 85% or 86% identity with SEQ ID Nos 1, 2 and 3 have not been described .

8. The variants recited in the claims must have at least 85% or 86% identity to one of SEQ ID NO 1, 2 or 3, but the variant nucleic acid molecules, polypeptides and antibodies that bind to the variant polypeptides may or may not evidence any enzymatic activity (claims 60-69 do not

claim the variants as having enzymatic activity (see rejection under 35 USC 112, second paragraph above), as only the reference molecules are required to evidence catalytic activity to hydrolyze urea in claims 60-70.

1. While specific species defined by specific nucleic acid sequences and complete amino acid sequences shown in Figure 1a have been disclosed, what the claimed variant nucleic acid molecules and polypeptides are, and what epitopes the antibodies bind on the variant polypeptides are has not been described..

Applicant also broadly describes the invention as embracing any substitution, insertion or deletion of amino acids throughout the entire stretch of nucleotides or amino acids found in the reference sequence by use of language in which only a "part" or "fragment" of the reference sequence is required, but the final relative molecular weight of the resultant protein is far larger than the region that can be selected from the reference proteins. None of the proteins that comprise any antigenic region of the recited sequence and reacts with an Helicobacter felis urease antibody, but differs by any number of amino acids, and has a sequence not represented by the sequences of SEQ ID NO 1, 2 or 3 and, encode or comprise amino acid sequences that do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The claimed nucleic acids and polypeptides that comprise sequences other than those set forth in Figure 1a, SEQ ID NO 1, 2 or 3, and do not evidence at least 95% identity to SEQ ID NO 1, 2 or 3 and also have enzymatic activity to catalyze the hydrolysis of urea have not been described. The specification does not provide original descriptive support for what the additional amino acid sequences are, that are in association with any number of parts, fragments or regions selected from each of the recited Helicobacter sequences.

The skilled artisan cannot envision all the contemplated nucleic acid molecules or polypeptides/proteins that encode or comprise any amino acid antigenic sequence region of Helicobacter felis ureaseXY. The detailed chemical structure of the claimed genus of proteins

has not been described and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. A method of screening for antigenic immunoreactivity is not a method of making a protein, the product itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. . Thus, the written description of the instant specification does not provide for "comprising" language. Therefore, only isolated nucleic acid molecules and polypeptides of SEQ ID Nos 1, 2 and 3 and those shown in Figure 1a have been described but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is serviceable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999. The rejection is maintained for reasons of record and responses set forth herein. This rejection could be partially obviated by amending the claims to recite---------95% identical----- and ----having catalyzing the hydrolysis of urea--------; or an equivalent phrase.

9. ***Claim Rejections - 35 USC § 102 Maintained.*** Claims 60-62, 67, 71-71, 75-76, 77-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Gootz et al (1994) as previously applied to claims 23,26,28,30, 33,34,37-39,40,44,57,58 and new claim 59.

10. Absent evidence to the contrary, the antibodies, polypeptides and nucleic acid of Gootz et al inherently are the antibodies, polypeptides and nucleic acids now claimed in light of the fact that Gootz et al produced the claimed and disclosed polypeptide, coding nucleic acid and antibodies by a different process to obtain the same or equivalent products. Gootz et al chose H.

felis ATCC 49179 (see abstract), also known as CS-1, the identical strain Applicant used to determine the sequence for urease as shown in Figure 1(a), SEQ Id NO 1 and isolated and purified the Helicobacter felis urease polypeptide (see Gootz et al, page 794, col. 1, paragraph 5), showed antibody compositions immunoreactive with the polypeptides (see Gootz et al, page 794, col. 2, paragraph 4, and Figure 3, page 795) and isolated the genes for H. felis urease in genomic blots of H.felis ATCC 49179 (see Figure 4), thus isolating the nucleic acid coding sequences for the H. felis urease polypeptides of CS-1.

11. While Gootz et al do not disclose the amino acid sequence, or nucleic acid sequences of the H. felis polypeptide and corresponding coding sequences for the H.felis CS-1 urease, by all comparable data the polypeptide, nucleic acid and antibodies immunoreactive to the polypeptide are the same or equivalent compositions now claimed produced by a different process, but obtained from the identical Helicobacter felis source as Applicants. The amino acid sequence and nucleic acid sequence of a polypeptide and nucleotide molecule, respectively, are descriptors of inherent structural residues of the polypeptide and DNA of Gootz et al. Discovery of a new descriptor of an already known product does not define a novel or unobvious product.

Gootz et al still inherently anticipates the instantly claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

This prior art rejection could be obviated by amending the claims to recite closed language -----**consisting of**---- and No longer recite the term ~~comprising~~ or ~~having.~~

New Grounds of Rejection

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 67-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 67-70 claim the nucleic acid molecule in the composition to be immunogenic. Are the variant nucleic acid molecules immunogenic or just the nucleic acids of SEQ ID NO 1? The instant Specification does not evidence original descriptive support for the instantly claimed genus of immunogenic nucleic acid molecules. Claims 67-70 recite New Matter.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 60-66, 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 60-66 recite the phrase "to nucleotides 206-2603 of SEQ ID NO 1 encoding a urease protein that catalyzes the hydrolysis of urea." While this phrase clearly describes nucleotides 206-2603 to encode an enzymatic active protein, what is the function of the variants that evidence "at least 85%" identity to nucleotides 206-2603 of SEQ ID NO 1? How can one of skill in the art determine the meets and bounds of the claim, if the variants do not have any biological activity and the sequences are variants of the reference sequence?

16. Claim 69 recites the limitation "antigen" in reference to claim 67 which recites the term "nucleic acid". There is insufficient antecedent basis for this limitation in the claim.

Conclusion

17. This is a non-final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vgp
June 18, 2007

MARK NAVARRO
PRIMARY EXAMINER